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PILLSBURY WINTHROP, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER
HELMS, LARRY RONALD

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1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No. 09/805,217	Applicant(s) BRAMS, PETER	
	Examiner Larry R. Helms	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *9-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1-8 and 27-28 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that the examiner upon determination that the subject antibodies are novel and non-obvious rejoin Group I with Group II. This is not found persuasive because applicants have not supplied any reasons why the restriction is improper. It is acknowledged that Groups I and II will be rejoined upon allowance of the Group I antibodies.

The requirement is still deemed proper and is therefore made **FINAL**.

2. Claims 9-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

3. Claims 1-8, 27-28 are under examination.

Specification

4. The disclosure is objected to because of the following informalities:

a. The first line of the specification should be updated to change the filing date of provisional application 60/189,050 from "March 14, 2001" to "March 14, 2000".

Appropriate correction is required.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claim 1 is rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter.

Claim 1 as written, do not sufficiently distinguish over antibodies as they exists naturally because claim 1 does not particularly point out any non-naturally occurring differences between the claimed antibodies and the structure of naturally occurring antibodies

In the absence of the hand of man, the naturally occurring antibodies are considered non-statutory subject matter (Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980)). It should be noted that the mere purity of a naturally occurring product does not necessarily impart patentability (Ex parte Siddiqui, 156 U.S.P.Q. 426 (1966)). However, when purification results in a new utility, patentability is considered (Merck Co. v. Chase Chemical Co., 273 F.Supp 68 (1967), 155 USPQ 139, (District Court, New Jersey, 1967)).

Claim 1 recite an antibody but do not recite that this protein is isolated or purified. It is well known that in autoimmune diseases, antibodies against self-antigens are generated and the claims as currently recited encompass these naturally-occurring compositions. Therefore, the antibody as claimed is a product that occurs in nature and does not show the hand of man, and as such is non-statutory subject matter. It is noted that in the specification on page 4 to page 5, line 2, anti-phospholipid antibodies which encompass PS antibodies have been found in patients with malignancies. Thus, auto antibodies have been found in patients and the claims encompass these antibodies.

Therefore, it is suggested that the claim be amended to recite "an isolated and purified antibody" to overcome this rejection.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 5-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5-8 are indefinite for reciting "treating tumors, neoplasms or cancer" in claim 5 because the exact meaning of the phrase is not clear. It is not clear how the terms are distinguished. For example how is the term tumor different from the term cancer or neoplasm?

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 3 and 7 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does

not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

It is unclear if a cell line which produces an antibody having the exact chemical identity of 2E7 is known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

For example, very different V_H chains (about 50% homologous) can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_K sequences to produce antibodies with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. [FUNDAMENTAL IMMUNOLOGY 242 (William E. Paul, M.D. ed., 3d ed. 1993)]. Therefore, it would require undue experimentation to reproduce the claimed antibody species 2E7. Deposit of the hybridoma would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See, 37 C.F.R. 1.801-1.809.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claim R j ctions - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Thorpe et al (U.S. Patent 6,312,694, filed 7/12/99 and has priority to 7/13/98).

The claims recite an anti-phosphatidyl serine antibody that binds phospholipid phosphatidyl serine wherein the antibody is a humanized monoclonal antibody and competes for binding with 2E7 and compositions comprising such and a kit comprising the antibody and . For this rejection the intended use of the antibody for treating tumors, neoplasms or cancer recited in claim 5 caries no patentable weight.

Thorpe et al teach anti-phosphatidyl serine antibodies (see column 14, lines 36-41) and the antibodies can be human or humanized or chimeric (see column 11-12) and compositions comprising such in a pharmaceutical acceptable carrier (see column 79, lines 10-32).

Although claims 3 and 7 recite an antibody that competes with 2E7, it is inherent that since the antibody of Thorpe et al binds phosphatidyl serine moiety and 2E7 also binds this moiety, it would be reasonable to conclude that the antibody of Thorpe et al would compete for binding with the 2E7 antibody.

13. Claim 1 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Maneta-Peyet et al (J. of Immunological Methods 108:123-127, 1988).

Claim 1 has been described supra. Claim 27 recites a kit comprising an antibody and ancillary reagents for detection. For this rejection the intended use of the kit for analyzing a sample for the presence of PS positive cells and detection carries no patentable weight

Maneta-Peyret et al teach an anti-phosphatidyl serine antibody (see abstract and entire document). Maneta-Peyret et al also teach an ELISA assay which comprises a anti-PS antibody and reagents such as plates and labeled antibodies for the detection of PS. Since claim 27 only requires the antibody and ancillary reagents, the art reads on the claims.

14. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Vogt et al (Am J. Obstet Gynecol 177:964-72, 1997).

The claims have been described supra.

Vogt et al teach a monoclonal antibody which binds phosphatidyl serine (see page 965, "Monoclonal aPL antibodies").

15. Claims 1-3, 5-7, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Umeda et al (The Journal of Immunology 143:2273-79, 1989).

The claims have been described supra. For this rejection the intended use of the antibody for treating tumors, neoplasms or cancer recited in claim 5 caries no patentable weight. For this rejection the intended use of the kit for analyzing a sample for the presence of PS positive cells and detection carries no patentable weight. Umeda et al teach monoclonal antibodies directed against phosphatidyl serine and compositions comprising such in HEPES buffer (see page 2274). Umeda et al also teach an ELISA assay for detection of PS comprising the anti-PS antibody and plates, and labeled antibodies (see page 2274). Since claim 27 only requires the antibody and ancillary reagents, the art reads on the claims.

Although claims 3 and 7 recite an antibody that competes with 2E7, it is inherent that since the antibody of Umeda et al binds phosphatidyl serine moiety and 2E7 also binds this moiety, it would be reasonable to conclude that the antibody of Umeda et al would compete for binding with the 2E7 antibody.

16. Claims 1-3, 5-7, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Rote et al (Clinical Immunology and Immunopathology 66:193-200, 1993).

The claims have been described supra. For this rejection the intended use of the antibody for treating tumors, neoplasms or cancer recited in claim 5 caries no patentable weight. For this rejection the intended use of the kit for analyzing a sample for the presence of PS positive cells and detection carries no patentable weight.

Rote et al teach monoclonal antibodies directed against phosphatidyl serine and compositions comprising such in PBS buffer (see abstract and page 194) and an ELISA assay for the detection of PS comprising an anti-PS antibody, plates, and labeled antibodies (see page 194). Since claim 27 only requires the antibody and ancillary reagents, the art reads on the claims.

Although claims 3 and 7 recite an antibody that competes with 2E7, it is inherent that since the antibody of Rote et al binds phosphatidyl serine moiety and 2E7 also binds this moiety, it would be reasonable to conclude that the antibody of Rote et al would compete for binding with the 2E7 antibody.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

18. Claims 1-8 and 27-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thorpe et al (U.S. Patent 6,312,694, filed 7/12/99 with priority to 7/13/98) as applied to claims 1-8 above, and further in view of Harlow et al (Antibodies, A Laboratory Manual, Cold Spring Harbor Laboratory, pages 390-91, 591, 592, 599, 601, 605, 608, 1988).

Claims 1-8 and 27 have been described supra. Claim 28 recites a kit further comprising a solid support, primary antibody, buffer to block the support, second labeled antibody, and positive and negative PS control cells. For this rejection the intended use of the antibody for treating tumors, neoplasms or cancer recited in claim 5 caries no patentable weight. For this rejection the intended use of the kit for analyzing a sample for the presence of PS positive cells and detection carries no patentable weight.

Thorpe et al has been described supra. Thorpe et al also teach PS is a stable marker on tumor vascular endothelial cells and PS-negative in blood vessels within normal tissues (see column 3, lines 10-15 and column 7, lines 8-10) and methods of diagnosis of tumors with antibodies and labeled antibodies (see column 12, column 21-22). Thorpe et al also teach methods of screening of antibodies using cells that express

the antigen and control cells (see column 57, lines 15-17) and general ELISA type assays (see column 78, lines 20-37) with solid supports and blocking reagents and secondary labeled antibodies. Thorpe et al does not exemplify a kit comprising the recited reagents and PS positive and negative control cells. These deficiencies are made up for in the teachings of Harlow et al.

Harlow et al teach general methods for antibody assays with cells with primary and secondary labeled antibodies and solid phase assays, and positive and negative control cells (see pages 390-91) and general ELISA assays and plates and blocking reagents and assay formats (see pages 591, 592, 599, 601, 605, 608).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the antibodies of Thorpe et al in an ELISA type assay as taught by Harlow et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the antibodies of Thorpe et al in an ELISA type assay as taught by Harlow et al because Thorpe et al teach assays with detection using an anti-Ps antibody and labeled antibodies and Thorpe et al teach that tumor cells are PS positive and normal cells are negative. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the antibodies of Thorpe et al in an ELISA type assay as taught by Harlow et al because Harlow et al teach cell based assays using ELISA type formats for detection of antigens and positive and negative controls should be used.

Although claims 27-28 recites a kit, no positive recitation of the kit ingredients/elements distinguishes the claim over the references. Therefore, the references read on the claimed kit. Further, it is a well-known convention in the art to place the recited elements in a kit for the advantages of convenience and economy, and methods of ELISA's for detection of antigens were well known and available to the ordinarily skilled artisan.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

19. No claim is allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

21. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879